General

Guideline Title

Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis.

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec 16. 57 p. (Technology appraisal guidance; no. 373).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Abatacept, adalimumab, etanercept and tocilizumab are recommended, within their marketing authorisations, as options for treating polyarticular juvenile idiopathic arthritis (JIA), including polyarticular-onset, polyarticular-course and extended oligoarticular JIA. That is:

- For abatacept, people 6 years and older whose disease has responded inadequately to other disease-modifying anti-rheumatic drugs (DMARDs) including at least one tumour necrosis factor (TNF) inhibitor
- For adalimumab, people 2 years and older whose disease has responded inadequately to one or more DMARD
- For etanercept, people 2 years and older whose disease has responded inadequately to, or who are intolerant of, methotrexate
- For tocilizumab, people 2 years and older whose disease has responded inadequately to previous therapy with methotrexate

Abatacept and tocilizumab are recommended only if the companies provide them with the discounts agreed in the patient access schemes for these technologies.

Adalimumab and etanercept are recommended, within their marketing authorisations, as options for treating enthesitis-related JIA, that is, for people 6 years and older (adalimumab) and 12 years and older (etanercept) whose disease has responded inadequately to, or who are intolerant of, conventional therapy.

Etanercept is recommended, within its marketing authorisation, as an option for treating psoriatic JIA, that is, in people aged 12 years and over whose disease has responded inadequately to, or who are intolerant of, methotrexate.

When more than one technology is suitable (taking into account extra-articular manifestations) treatment should be started with the least expensive technology, taking into account administration costs, the dose needed and the product cost per dose.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Juvenile idiopathic arthritis (JIA) including polyarticular-onset, polyarticular-course and extended oligoarticular JIA; enthesitis-related JIA; and psoriatic JIA

Guideline Category

Assessment of Therapeutic Effectiveness

Treatment

Clinical Specialty

Family Practice

Pediatrics

Rheumatology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To evaluate the clinical effectiveness and cost-effectiveness of abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis (JIA)

Target Population

Patients with juvenile idiopathic arthritis (JIA)

Interventions and Practices Considered

1. Abatacept
2. Adalimumab

3. Etanercept
4. Tocilizumab

Major Outcomes Considered

- Clinical effectiveness
  - Disease activity
  - Disease flares
  - Physical function
  - Joint damage
  - Pain
  - Corticosteroid reducing regimens
  - Extra-articular manifestations (such as uveitis)
  - Body weight and height
  - Mortality
  - Adverse effects of treatment
  - Health-related quality of life (HRQoL)
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the technology considered in this appraisal and prepare an Assessment Report. The Assessment Report for this technology appraisal was prepared by Southampton Health Technology Assessments Centre (SHTAC) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Methods

The *a priori* methods for systematically reviewing the evidence of clinical effectiveness and cost-effectiveness are described in a research protocol published on the NICE Web site and registered with the PROSPERO international prospective register of systematic reviews database. The protocol was sent to the expert advisory group for comment. Minor amendments were made as appropriate. None of the comments received identified specific problems with the methods of the review.

Identification of Studies

Sensitive search strategies were developed and refined by an experienced information specialist. Separate searches were conducted to identify studies of clinical-effectiveness, cost-effectiveness and health-related quality of life (HRQoL).

The following databases were searched for published studies and ongoing research from inception to May 2015: The Cochrane Library including the Cochrane Database of Systematic Reviews (CDSR), the Cochrane Central Register of Controlled Trials, the Centre for Reviews and

Dissemination (CRD, University of York) Database of Abstracts of Reviews of Effectiveness (DARE), National Health Service Economic Evaluation Database (NHS EED), and the Health Technology Assessment (HTA) database; EMBASE (Ovid); MEDLINE(R) (Ovid); MEDLINE In-Process and Other Non-Indexed Citations (Ovid); Web of Science with Conference Proceedings: Science Citation Index Expanded (SCIE) and Conference Proceedings Citation Index - Science (CPCI) (ISI Web of Knowledge); Biosis Previews (ISI Web of Knowledge); Zetoc (Mimas); National Institute for Health Research (NIHR)-Clinical Research Network Portfolio; Clinical Trials.gov, ISRCTN (International Standard Randomised Clinical Trial Number), UKCTG (UK Clinical Trials Gateway) and World Health Organisation (WHO) ICTRP (International Clinical Trials Research Platform). In addition, PsycINFO (Ebsco) was searched for HRQoL studies. Searches were not limited to particular trial designs and although searches were not restricted by language, only full texts of English-language articles were retrieved during the study selection process. Cost-effectiveness and HRQoL searchers were conducted from database inception to May 2015. References were downloaded into a Reference Manager database and de-duplicated where necessary.

Bibliographies of included articles and systematic reviews were also searched. The company submissions (CS) to NICE were searched for any additional studies that met the inclusion criteria. Members of the advisory group were asked to identify additional published and unpublished evidence. Further details including search dates for each database and an example search strategy can be found in Appendix 1 of the Assessment Report.

Inclusion and Exclusion Criteria

The following inclusion/exclusion criteria were applied to the clinical-effectiveness review:

- *Interventions*: Etanercept, abatacept (with or without methotrexate), adalimumab (with or without methotrexate) and tocilizumab (with or without methotrexate). Each drug was evaluated within their licensed indication. Studies of treatment without methotrexate were permitted if patients were intolerant to methotrexate or for whom treatment with methotrexate is inappropriate.
- *Comparators*: Disease-modifying anti-rheumatic drugs (DMARDs) (such as methotrexate, which is the most common conventional treatment in the UK) if DMARDs can be tolerated and best supportive care if DMARDs are not tolerated. Etanercept, abatacept, adalimumab and tocilizumab compared with each other.
- *Population*: Patients with juvenile idiopathic arthritis (JIA) including: Polyarthritis (rheumatoid factor +ve, rheumatoid factor -ve and extended oligoarthritis, both onset and course); enthesitis-related arthritis (ERA); psoriatic arthritis (PA). Studies of patients with systemic JIA were not included, as this was the subject of a separate NICE appraisal.
- *Outcomes*: Studies reporting one or more of the following outcomes were included: Disease activity, disease flares, physical function, joint damage, pain, corticosteroid reducing regimens, extra-articular manifestations (such as uveitis), body weight and height, mortality, adverse effects of treatment, HRQoL.
- *Study design*: Randomised controlled trials (RCTs). Any relevant systematic reviews identified in the systematic review of clinical-effectiveness were used as a source of references. Studies published as abstracts or conference presentations were only included if published from 2012 onwards and sufficient details were presented (or available elsewhere, e.g., in a full paper reporting on the same RCT) to allow an appraisal of the methodology and the assessment of results to be undertaken.

Reference Screening

All studies were selected for inclusion through a two-stage process. Titles and abstracts were screened independently by two reviewers for potential eligibility, using a standardised and piloted eligibility selection worksheet (see Appendix 2 of the Assessment Report) containing the inclusion/exclusion criteria detailed above.

Full Paper Screening

Full texts for potentially relevant studies were obtained and screened using a standardised and piloted eligibility section worksheet (see Appendix 3 of the Assessment Report) by one reviewer, checked by a second and a final decision regarding inclusion was agreed. At each stage any disagreements were resolved by discussion or with the involvement of a third reviewer when necessary.

Results

Titles and, where available, abstracts of a total of 2651 references identified by searches (after deduplication) were screened and full copies of 60 references were retrieved. Of these 29 were excluded after inspection of the full article as shown in Figure 1 of the Assessment Report, and these are listed in Appendix 4 of the Assessment Report. The most common reason for exclusion of a reference was an irrelevant study design (e.g., systematic reviews [which were used as a source of references], commentaries). One full text was of unclear relevance to the review because the type of JIA was not stated and it was not clear whether participants met the licenced indication for etanercept therapy in respect of having inadequate response or intolerance to methotrexate.

Nine full texts and 12 conference abstracts described four RCTs (each described by at least one full paper) that met the inclusion criteria of the review (see Figure 1 of the Assessment Report). As the full texts provided the most complete data, these were the primary source of information for this review.

Economic Analysis

Systematic Review of Cost-effectiveness Evidence

Methods for the Systematic Review

A systematic literature search was undertaken to identify economic evaluations of the biologic DMARDs, within the NICE scope for this appraisal. Studies were included if they were full economic evaluations (cost-effectiveness, cost-utility, cost-consequence, or cost-benefit analyses) conducted in children and young people with JIA that compared one or more biologics with a DMARD, such as methotrexate. Studies that were not reported in the English language or did not provide sufficient information on the model structure, data and results were excluded. This systematic review aimed to summarise the currently available evidence and inform the construction of a *de novo* model.

Results of the Systematic Review

Searches for economic evaluations identified 387 potentially relevant references and a further study was identified through *ad hoc* searching. The full texts for 17 papers were retrieved for further screening. A summary of the selection process and the reasons for exclusion are presented in Figure 6 and a list of excluded studies in Appendix 6 of the Assessment Report. Although seven studies reported as abstracts appeared to meet the *a priori* inclusion criteria, they did not contain sufficient information on the methods used and the results to permit formal data extraction or critical appraisal. Five studies were found not to be economic evaluations. Four studies were included, described in a total of five publications. The characteristics of the four included economic evaluations are shown in Table 38 of the Assessment Report.

See Figure 6 of the Assessment Report for the flow chart of identification of studies for inclusion in the review of cost-effectiveness.

Systematic Review of Health-related Quality of Life Studies (HRQoL)

Methods for the Systematic Review

A systematic literature review was undertaken to assess the HRQoL of people with JIA treated with biologic DMARDs. The aim of the review was to provide data to populate the *de novo* economic model in this report with health state utility values to calculate quality-adjusted life years (QALYs). The description of the search strategy is shown in Appendix 1 of the Assessment Report. The inclusion criteria were to include primary studies that investigated HRQoL in people with JIA. To be eligible, the study should report health utility values using any generic preference based HRQoL measure (e.g., EurQual-5D [EQ-5D], Short-Form 36 [SF-6D]) or choice-based valuation methods (e.g., time trade off, standard gamble). Studies that were not reported in the English language or did not provide sufficient information were excluded.

Results of the Systematic Review

The database searches identified 2249 references, with one further study retrieved by hand searching, making the total references identified 2250. Full text papers for 28 references were retrieved, meeting the *a priori* inclusion criteria. Figure 7 of the Assessment Report presents a flow chart of the selection process and the excluded studies with reasons for exclusion are listed in Appendix 7 of the Assessment Report. Six references were considered to have insufficient information on the study methods, population and results, nine included an inappropriate population and ten did not report a relevant outcome measure. Two studies, described in three publications, met the inclusion criteria and the characteristics of these studies are presented in Table 40 of the Assessment Report.

Number of Source Documents

Clinical Effectiveness

Nine full papers and 12 conference abstracts were included.

- Abatacept - 1 study (3 papers, 1 abstract)
- Adalimumab - 1 study (1 paper, 3 abstracts)
- Etanercept - 1 study (4 papers)
- Tocilizumab - 1 study (1 paper, 8 abstracts)

Economic Analysis

- *Cost-effectiveness*: Four studies described in five publications were included.
- *Health-related quality of life (HRQoL)*: Two studies, described in three publications, met the inclusion criteria.
- The manufacturers of abatacept and tocilizumab submitted economic models. An independent economic model was also submitted by the Assessment Group.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): The National Institute for Health and Care Excellence (NICE) commissioned an independent academic centre to perform an assessment of the technology considered in this appraisal and prepare an Assessment Report. The Assessment Report for this technology appraisal was prepared by Southampton Health Technology Assessments Centre (SHTAC) (see the "Availability of Companion Documents" field).

Clinical Effectiveness

Critical Appraisal Strategy

Clinical effectiveness studies were appraised using the Cochrane Risk of Bias criteria (e.g., selection bias, detection bias, performance bias, attrition bias, and selective reporting bias). Aspects of study quality including statistical procedures, outcome measurement and generalisability were also assessed.

Critical appraisal of the included clinical effectiveness and cost-effectiveness studies (see below) was conducted by one reviewer and checked by a second reviewer. Any disagreements were resolved by consensus or in consultation with a third reviewer where necessary.

Method of Data Synthesis

Details of the trial outcomes in the clinical effectiveness review were synthesised through narrative review with tabulation of the results of included studies. Quantitative pooling of outcomes across clinical effectiveness studies in a meta-analysis was not possible as the identified evidence included only one trial per biologic disease-modifying anti-rheumatic drug (DMARD), all using placebo as the comparator. It was not considered appropriate to meta-analyse the four biologic DMARDs together due to clinical heterogeneity.

An adjusted indirect comparison of the four biologic DMARDs was performed using the method described by Bucher and colleagues (1997). An indirect comparison refers to the synthesis of data from trials in which the technologies of interest have not been compared in head-to-head trials, but have been compared indirectly using data from a network of trials that compare the technologies with other interventions. A distinction is often made between adjusted and naïve (unadjusted) indirect comparisons. In the adjusted indirect comparison, the comparison of the interventions of interest is adjusted by preserving the strength of randomisation. Unadjusted indirect comparisons are considered to be observational evidence and therefore not recommended.

See Section 4 of the Assessment Report for additional information on clinical effectiveness analysis.

Economic Analysis

Critical Appraisal of the Studies

The cost-effectiveness studies were assessed using a critical appraisal checklist (Table 39 of the Assessment Report). The checklist assessed study quality and generalisability to the UK. The checklist was adapted by the review authors from checklists by Philips and colleagues, Drummond and colleagues and methodological requirements stated in the NICE reference case.

Review of Cost-effectiveness in Company Submissions to NICE

All four pharmaceutical companies submitted evidence to be considered for the NICE appraisal. Two of these submissions (BMS [abatacept] and Roche [tocilizumab]) consisted of a written report and an electronic economic model, and the other two submissions (AbbVie [adalimumab] and Pfizer [etanercept]) just comprised a written report.

A structured data extraction form was used by the assessment group to assess the company submissions (see Appendix 10 of the Assessment Report). A description and critique of each of the submissions in turn is provided in Section 5 of the Assessment Report. Greater description is provided of the Roche and the BMS submissions as these conducted economic models. (Note: a description and critique of the companies' clinical effectiveness evidence is given in Section 4.2 of the Assessment Report.)

Independent Economic Evaluation

The models described in the systematic review of economic evaluations (Section 5.2 of the Assessment Report) had certain methodological limitations and were not wholly generalisable to the National Health Service (NHS). Furthermore, the economic evaluation used to inform the NICE appraisal of tocilizumab for systemic juvenile idiopathic arthritis (JIA) was subject to a number of concerns from the Appraisal Committee, especially with regard to the estimation of health-related quality of life (HRQoL). Given the limitations of existing available models, the Assessment Group therefore constructed a *de novo* economic model to inform this current appraisal.

The model estimates the costs, benefits and cost-effectiveness of the four biologic DMARDs in patients with JIA and inadequate responses to, or intolerance of, methotrexate. The model compares the biologic DMARDs (in combination with methotrexate, where permitted) with a DMARD (e.g., methotrexate), as specified in the NICE scope. The model does not compare the biologic DMARDs with best supportive care (e.g., nonsteroidal anti-inflammatory drugs [NSAIDS]; corticosteroids) for patients who cannot tolerate a DMARD as there are limited data available to make this comparison. Furthermore, patients who are intolerant to a DMARD such as methotrexate would be offered a biologic DMARD rather than best supportive care, particularly to avoid potential adverse effects of long-term corticosteroid use.

See Section 5 of the Assessment Report for additional descriptions of the economic evaluation.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Considerations

Technology appraisal recommendations are based on a review of clinical and economic evidence.

Technology Appraisal Process

The National Institute for Health and Care Excellence (NICE) invites 'consultee' and 'commentator' organisations to take part in the appraisal process. Consultee organisations include national groups representing patients and carers, the bodies representing health professionals, and the manufacturers of the technology under review. Consultees are invited to submit evidence during the appraisal and to comment on the appraisal documents.

Commentator organisations include manufacturers of the products with which the technology is being compared, the National Health Service (NHS) Quality Improvement Scotland and research groups working in the area. They can comment on the evidence and other documents but are not asked to submit evidence themselves.

NICE then commissions an independent academic centre to review published evidence on the technology and prepare an 'Assessment Report. Consultees and commentators are invited to comment on the report. The assessment report and the comments on it are then drawn together in a document called the evaluation report.

An independent Appraisal Committee then considers the evaluation report. It holds a meeting where it hears direct, spoken evidence from

nominated clinical experts, patients and carers. The Committee uses all the evidence to make its first recommendations, in a document called the Appraisal Consultation Document (ACD). NICE sends all the consultees and commentators a copy of this document and posts it on the NICE Web site. Further comments are invited from everyone taking part.

When the Committee meets again it considers any comments submitted on the ACD; then it prepares its final recommendations in a document called the Final Appraisal Determination (FAD). This is submitted to NICE for approval.

Consultees have a chance to appeal against the final recommendations in the FAD. If there are no appeals, the final recommendations become the basis of the guidance that NICE issues.

Who Is on the Appraisal Committee?

NICE technology appraisal recommendations are prepared by an independent committee. This includes health professionals working in the NHS and people who are familiar with the issues affecting patients and carers. Although the Appraisal Committee seeks the views of organisations representing health professionals, patients, carers, manufacturers and government, its advice is independent of any vested interests.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

Summary of Appraisal Committee's Key Conclusions

Availability and Nature of Evidence

The Assessment Group produced 2 cost-effectiveness models (1 for when the technologies were taken as the first biological treatment and 1 for when they were taken after a biological treatment). The manufacturer of tocilizumab submitted a cost-effectiveness model comparing tocilizumab with adalimumab. Additional comments on cost-effectiveness modelling were received from the manufacturers of abatacept, adalimumab and etanercept.

Uncertainties Around and Plausibility of Assumptions and Inputs in the Economic Model

The Assessment Group's model did not fully capture the benefits of the biological treatments in reducing disease activity because it modelled disease flare only, without additionally modelling disease response.

Additional possible clinical benefits of the technologies were not modelled, including uveitis, preventing long-term joint damage, avoiding surgery and minimising the adverse effects of corticosteroids. It was not possible to estimate the extent of these potential benefits.

Incorporation of Health-related Quality-of-Life Benefits and Utility Values. Have Any Potential Significant and Substantial Health-related Benefits Been Identified That Were Not Included in the Economic Model, and How Have They Been Considered?

There was considerable uncertainty surrounding the utility values used in the model because of the lack of data. It is reasonable that quality of life should increase over time if the disease is well controlled, and should decrease if the disease remains uncontrolled, but this was not fully captured in the modelling. It was relevant to include caregiver utility in the modelling.

Are There Specific Groups of People for Whom the Technology Is Particularly Cost Effective?

No

What Are the Key Drivers of Cost-effectiveness?

The additional possible clinical benefits of the technologies, which were not modelled, were expected to reduce the incremental cost-effectiveness ratios (ICERs) had they been included. Although it was not possible to quantify the exact impact of these factors, it was considered likely that they would bring the ICERs into a range considered a cost-effective use of National Health Service (NHS) resources if the innovative nature of the technologies was also taken into account.

Most Likely Cost-effectiveness Estimate (Given as ICER)

The ICERs for all 4 technologies compared with methotrexate were expected to be lower than those estimated by the Assessment Group's model, including the Committee's preferred scenarios (just below £30,000 per quality-adjusted life year [QALY] gained or at the lower end of a £30,000 to £40,000 per QALY gained range). Including potential clinical benefits not modelled would be expected to reduce these ICERs further.

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Consultee organisations from the following groups were invited to comment on the draft scope, Assessment Report and the Appraisal Consultation Document (ACD) and were provided with the opportunity to appeal against the Final Appraisal Determination (FAD).

- Manufacturer/sponsors
- Professional/specialist and patient/carer groups
- Commentator organisations (without the right of appeal)

In addition, individuals selected from clinical expert and patient advocate nominations from the professional/specialist and patient/carer groups were also invited to comment on the ACD.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

The Appraisal Committee considered clinical and cost-effectiveness evidence for abatacept, adalimumab, etanercept, and tocilizumab from a systematic review and economic evaluation prepared by an independent assessment group. The main clinical effectiveness evidence came from four randomised controlled trials (RCTs).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- The systematic review of clinical effectiveness conducted for the Evidence Review Group (ERG) report found that biologic disease-modifying anti-rheumatic drugs (DMARDs) are superior to placebo (with methotrexate where permitted) across a number of outcome measures in children with JIA (predominantly polyarticular course) and who had an insufficient response to previous DMARD treatment.
- These biological treatments have reduced long-term use of corticosteroids in clinical practice, which are associated with side effects.

Potential Harms

- The summary of product characteristics lists upper respiratory tract infections as the only very common (affecting 1 in 10 people or more) adverse reaction for abatacept.
- The summary of product characteristics lists the following very common (affecting 1 in 10 people or more) adverse reactions for adalimumab: respiratory tract infections, low white blood cell count, low red blood cell count, increased blood levels of lipids, headache, abdominal pain, nausea and vomiting, rash, musculoskeletal pain, injection site reactions and increased plasma levels of liver enzymes.
- The summary of product characteristics lists the following very common (affecting 1 in 10 people or more) adverse reactions for etanercept: injection site reactions, upper respiratory tract infections, and bladder and skin infections.
- The summary of product characteristics lists the following adverse reactions affecting 5 people in 100 or more for tocilizumab: upper respiratory tract infections, nasopharyngitis, headache, hypertension and abnormal liver function tests.

For full details of adverse reactions and contraindications, see the summary of product characteristics.

Contraindications

Contraindications

For full details of contraindications, see the summary of product characteristics.

Qualifying Statements

Qualifying Statements

- This guidance represents the views of the National Institute for Health and Care Excellence (NICE) and was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.
- Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

Implementation of the Guideline

Description of Implementation Strategy

- Section 7(6) of the National Institute for Health and Care Excellence (NICE) (Constitution and Functions) and the Health and Social Care Information Centre (Functions) Regulations 2013 requires clinical commissioning groups, National Health Service (NHS) England and, with respect to their public health functions, local authorities to comply with the recommendations in this appraisal within 3 months of its date of publication.
- The Welsh Assembly Minister for Health and Social Services has issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 3 months of the guidance being published.
- When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient has juvenile idiopathic arthritis and the doctor responsible for their care thinks that abatacept, adalimumab, etanercept or tocilizumab is the right treatment, it should be available for use, in line with NICE's recommendations.
- The Department of Health and Bristol-Myers Squibb have agreed that abatacept will be available to the NHS with a patient access scheme which makes it available with a discount. The Department of Health and Roche have agreed that tocilizumab will be available to the NHS with a patient access scheme which makes it available with a discount. The size of these discounts is commercial in confidence. It is the responsibility of each company to communicate details of the discount to the relevant NHS organisations. Any enquiries from NHS organisations about the patient access scheme for tocilizumab (RoActemra) should be directed to the Roche Customer Care (0800731 5711). Any enquiries from NHS organisations about the patient access scheme for abatacept (Orencia) should be directed to BMS Customer Services (Chester) on 01244 586250, or to the following email address: ukpasadmin@bms.com.
- NICE has developed tools to help organisations put this guidance into practice (listed below).
    - A costing statement explaining the resource impact of this guidance

Implementation Tools

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Institute for Health and Care Excellence (NICE). Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec 16. 57 p. (Technology appraisal guidance; no. 373).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2015 Dec 16

Guideline Developer(s)

National Institute for Health and Care Excellence (NICE) - National Government Agency [Non-U.S.]

Source(s) of Funding

National Institute for Health and Care Excellence (NICE)

Guideline Committee

Appraisal Committee

Composition of Group That Authored the Guideline

Committee Members: Dr Amanda Adler (*Chair*), Consultant Physician, Addenbrooke's Hospital; Professor Ken Stein (*Vice Chair*), Professor of Public Health, University of Exeter Medical School; Dr Ray Armstrong, Consultant Rheumatologist, Southampton General Hospital; Dr Jeff Aronson, Reader in Clinical Pharmacology, University Department of Primary Health Care, University of Oxford; Mr Matthew Campbell-Hill, Lay member; Mr Mark Chapman, Health Economics and Market Access Manager, Medtronic UK; Dr Peter Crome, Consultant, Geriatrics; Dr Neil Iosson, Locum General Practitioner; Mrs Anne Joshua, NHS 111 Pharmacy Lead, Patients and Information, NHS England; Dr Sanjay Kinra, Reader in Clinical Epidemiology and Honorary Consultant in Paediatrics, London School of Hygiene and Tropical Medicine and University College London NHS Hospitals Trust; Mr Christopher O'Regan, Head of Health Technology Assessment & Outcomes Research, Merck Sharp & Dohme; Professor Stephen Palmer, Professor of Health Economics, Centre for Health Economics, University of York; Dr Sanjeev Patel, Consultant Physician & Senior Lecturer in Rheumatology, St Helier University Hospital; Dr John Pounsford, Consultant Physician, Frenchay Hospital, Bristol; Dr Nicky Welton, Senior Lecturer in Biostatistics/Health Technology Assessment, University of Bristol

Financial Disclosures/Conflicts of Interest

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that appraisal.

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available for download in ePub and eBook formats from the NICE Web site.

Availability of Companion Documents

The following are available:

- Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis. Resource impact report. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec. 1 p. (Technology appraisal guidance; no. 373). Available from the National Institute for Health and Care Excellence (NICE) Web site.
- Shephard J, Cooper K, Harris P, Picot J, Rose M. The clinical and cost-effectiveness of abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis: a systematic review and economic evaluation. Southampton (UK): Southampton Health Technology Assessments Centre (SHTAC); 2015 Jul. 232 p. Available from the NICE Web site.

Patient Resources

The following is available:

- Abatacept, adalimumab, etanercept and tocilizumab for treating juvenile idiopathic arthritis. Information for the public. London (UK): National Institute for Health and Care Excellence (NICE); 2015 Dec. 3 p. (Technology appraisal guidance; no. 373). Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available for download in ePub and eBook formats from the NICE Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a

licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on March 28, 2016.

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